REMARKS

Applicants respectfully request entry of the amendment and reconsideration of the claims. Claims 49 and 59 have been amended to further clarify the invention as claimed. Claims 1, 36-48, 51-56, and 60-68 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the cancelled subject matter in a continuation application. After entry of the amendment, claims 35, 49, 50, and 57-59 will be pending.

Applicants submit the amendment is supported throughout the specification, including for example at page 26, lines 23-26, 27, line 28 to page 28, line 1, page 67, lines 2-5, and Figs. 1, 2, and 4, and does not raise any issues of new matter.

35 U.S.C. § 112, first paragraph

Claims 35, 49, 50, and 57-59 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse this rejection.

The Office Action alleges the specification does not enable agonist antibodies that bind TCCR variants having 80% identity to SEQ ID NO:1. Without acquiescing to the rejection and solely for the purpose of advancing prosecution, Applicants have amended the claims to recite that TCCR comprises an amino acid sequence of SEQ ID NO:1. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

The Office Action alleges the specification does not enable monovalent agonist antibodies. The Office Action, however, acknowledges that agonist antibodies were known, that strategies for developing agonist antibodies were known, and that intact antibodies and antibody fragments that retain at least two antigen binding sites can act as agonists of cytokine receptor molecules by crosslinking receptor molecules.

Without acquiescing to the rejection and solely for the purpose of advancing prosecution, the claims have been amended to recite that a fragment of a TCCR agonist antibody comprises two or more TCCR antigen binding sites. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

In view of the forgoing, Applicants submit the claims as amended fully comply with 35 U.S.C. § 112, first paragraph. Withdrawal of the enablement rejection is respectfully requested.

35 U.S.C. § 102(b)

Claims 35, 49, 50 and 57 were rejected under 35 U.S.C. § 120(b) as anticipated by Baumgartner (U.S. 5,792, 850). Applicants respectfully traverse this rejection.

In order to anticipate a claim, the prior art reference must teach each and every element of the claim. *See* MPEP 2131.01, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The identical invention must be shown in the same complete detail as is recited by the claims. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989). Applying these standards, Applicants submit the Baumgartner reference does not disclose all the elements of the claims.

Baumgartner discloses Zcytor 1 (SEQ ID NO:5), which is 100% identical to TCCR as shown by SEQ ID NO:1 in the specification. The reference discloses that agonists of Zcytor 1 may be useful for stimulating cell-mediated immunity and stimulating lymphocyte proliferation. See, for example, Baumgarnter at column 15, lines 3-5. With respect to stimulating lymphocyte proliferation with a Zcytor 1 agonist, Baumgartner does not distinguish between T cells and B cells, or Th0 cells, Th1 cells, and Th2 cells.

Applicants' claims are drawn to methods of inhibiting or attenuating differentiation of Th0 cells into a Th2 subtype comprising administering to the Th0 cells an effective amount of a TCCR agonist. Inhibiting or attenuating differentiation of Th2 cells in effect inhibits or attenuates proliferation of Th2 cells. Baumgartner does not teach or suggest the claimed method of administering a TCCR or Zcytor 1 agonist to inhibit differentiation, and thereby inhibit proliferation, of Th2 cells. Rather, Baumgartner discloses that an agonist of Zcytor 1 would stimulate lymphocyte proliferation. Baumgartner therefore does not disclose all the elements of the claims.

As discussed above, Baumgartner discloses that agonists of Zcytor 1 may be useful for stimulating cell-mediated immunity. Th2 cells, however, are associated with humoral immunity, not cell-mediated immunity. See, for example, Fig. 1 in the specification. The claims are directed to administering a TCCR agonist to attenuate or inhibit production of Th2 cells. The claims therefore encompass inhibiting or attenuating humoral immunity with a TCCR agonist.

Baumgartner does not teach or suggest inhibiting or attenuating humoral immunity with a TCCR or Zcytor 1 agonist.

In view of the foregoing, Applicants submit the claims are not anticipated by Baumgartner. The reference does not disclose all the elements of the claims for the reasons discussed above. Withdrawal of the rejection is respectfully requested.

35 U.S.C. § 103(a)

Claims 35, 49, 50, and 57-59 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Baumgartner in view of Queen (U.S. 5,585,089) and Holliger (U.S. 5,837,242). Applicants respectfully traverse this rejection.

To make a *prima facie* case of obviousness, the teachings of the prior art should have suggested the claimed subject matter to the person of ordinary skill in the art, and all the claim limitations must be taught or suggested in the references cited by the Examiner. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). As articulated by the Supreme Court in a recent case, a combination is obvious if it is no more than the predictable use of known elements according to their established functions and there was a reason to combine the known elements. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. __ (2007). To make a *prima facie* case of obviousness, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." *Id.* A "reasonable expectation of success" is the standard with which obviousness is determined. MPEP § 2141; *Hodosh v. Block Drug Co.*, 786 F.2d 182, 187 n.5 (Fed. Cir. 1986).

The initial burden to make a *prima facie* case of obviousness is on the Examiner. *In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). Applicants submit the Office Action has not established a *prima facie* case of obviousness because the Office Action has failed to establish that one of skill in the art in view of the cited combination of references had a reasonable expectation of successfully arriving at Applicants' claims.

As discussed above, Baumgartner discloses that agonists of Zcytor 1 may be useful for stimulating lymphocyte proliferation in general. With respect to the alleged effects of Zcytor 1 agonists on lymphocytes, Baumgartner does not distinguish between T cells and B cells, or Th0

cells, Th1 cells, and Th2 cells. In contrast to Baumgartner, Applicants' claims are drawn to methods of inhibiting or attenuating differentiation of Th0 cells into a Th2 subtype comprising administering to the Th0 cells an effective amount of a TCCR agonist. Inhibiting or attenuating differentiation of Th2 cells in effect inhibits or attenuates proliferation of Th2 cells. Baumgartner discloses administering a Zcytor 1 agonist to stimulate lymphocyte proliferation and therefore teaches away from the claims.

The secondary references of Queen and Holliger do not cure the deficiencies of Baumgartner. Neither secondary reference teaches or suggests administering a TCCR agonist or Zcytor agonist to inhibit or attenuate the differentiation or proliferation of Th2 cells. Therefore, one of skill in the art in view of the cited combination of references would not have had a reasonable expectation of successfully arriving at Applicants' claims.

As discussed above, Baumgartner discloses that agonists of Zcytor 1 may be useful for stimulating cell-mediated immunity. Th2 cells, however, are associated with humoral immunity, not cell-mediated immunity. The claims are directed to administering a TCCR agonist to attenuate or inhibit production of Th2 cells. Baumgartner does not teach or suggest administering a TCCR agonist or Zcytor 1 agonist to inhibit or attenuate humoral immunity. The secondary references of Queen and Holliger do not cure the deficiencies of the Baumgartner. Neither secondary reference teaches or suggests administering a TCCR agonist or Zcytor 1 agonist to inhibit or attenuate humoral immunity. Therefore, one of skill in the art in view of the cited combination of references would not have had a reasonable expectation of successfully arriving at Applicants' claims.

In view of the foregoing, Applicants submit the Office Action has failed to establish a *prima facie* case of obviousness. The Baumgartner reference teaches away from the claims, and the cited combination of references fails to teach or suggest all the elements of the claims. Absent Applicants' disclosure, one of skill in the art would not have been motivated to administer a TCCR agonist to inhibit or attenuate differentiation of Th0 cells into Th2 cells. Withdrawal of the rejection is respectfully requested.

Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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